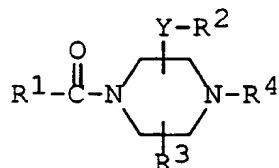


## C L A I M S

1. A compound of the formula :



wherein

Y is bond or lower alkylene,

R<sup>1</sup> is aryl which is substituted with 1 to 3 same or different substituent(s) selected from the group consisting of halogen, lower alkyl, lower alkoxy, mono(or di or tri)halo(lower)alkyl, nitro, amino, lower alkylamino, di(lower)alkylamino, lower alkylthio, lower alkylsulfonyl, cyclo(lower)alkylsulfonyl, aminosulfonyl, lower alkylaminosulfonyl, di(lower)alkylaminosulfonyl, pyrrolidinylsulfonyl, morpholinylsulfonyl, pyrrolylsulfonyl, pyridylsulfonyl, pyrrolyl and pyridyl;

R<sup>2</sup> is aryl which is substituted with 1 to 3 same or different substituent(s) selected from the group consisting of lower alkyl, mono(or di or tri)halo(lower)alkyl, mono(or di or tri)halo(lower)alkylsulfonyloxy, halogen, lower alkylenedioxy, lower alkoxy, lower alkoxycarbonyl, lower alkoxy(lower)alkoxy(lower)alkoxy, hydroxy, diphenyl(lower)alkylsilyloxy, tri(lower)alkylsilyloxy, hydroxy(lower)alkyl, cyano, amino, [mono(or di or tri)halo(lower)alkylcarbonyl]amino, lower alkylamino, N-(lower alkyl)-[mono(or di or

tri)halo(lower)alkylcarbonylamino, pyrrolidinyl  
and morpholinyl which may be substituted with lower  
alkoxy(lower)alkyl or lower alkyl;

R<sup>3</sup> is hydrogen or lower alkyl; and

R<sup>4</sup> is (3-pyridyl)methyl;

(3-pyridyl)ethyl;

3-(3-pyridyl)propyl;

3-(3-pyridyl)propenyl;

3-(3-pyridyl)propynyl;

thiazolyl(lower)alkyl, 1,2,4-

thiadiazolyl(lower)alkyl or 1,2,4-

oxadiazolyl(lower)alkyl, each of which is

substituted with halogen, amino, lower alkylamino  
or di(lower)alkylamino;

pyrazolylmethyl which may be substituted with

triphenyl(lower)alkyl or hydroxy(lower)alkyl;

pyrazolyl(lower)alkyl which is substituted with  
lower alkyl,

lower alkoxy(lower)alkylmorpholinyl(lower)alkyl or

lower alkoxy(lower)alkylmorpholinylcarbonyl-

(lower)alkyl;

pyrrolidinyl(lower)alkyl which is substituted with

1 or 2 same or different substituent(s) selected

from the group consisting of hydroxy,

hydroxy(lower)alkyl, lower alkoxy and lower

alkoxy(lower)alkyl;

piperidylmethyl;

piperidyl(lower)alkyl which is substituted with 1

or 2 same or different substituent(s) selected from

the group consisting of halogen, lower alkyl and

lower alkoxy(lower)alkyl;

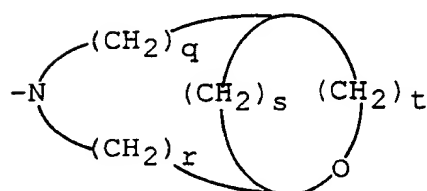
[2,6-di(hydroxy(lower)alkyl)piperidyl](lower)alkyl;

(2,6-dimethylmorpholino)(lower)alkyl;

(2,2-dimethylmorpholino)(lower)alkyl;

(3,3-dimethylmorpholino)(lower)alkyl;

(cis-3,5-dimethylmorpholino) (lower) alkyl;  
 ((3S,5S)-3,5-dimethylmorpholino) (lower) alkyl;  
 ((3S,5R)-3,5-dimethylmorpholino) (lower) alkyl;  
 (2-methoxymethylmorpholino) (lower) alkyl;  
 (3-methoxymethylmorpholino) (lower) alkyl;  
 (2-methoxymethyl-5-methylmorpholino) (lower) alkyl;  
 (2-methoxymethyl-5,5-dimethylmorpholino) (lower) -  
 alkyl;  
 (3,5-dimethoxymethylmorpholino) (lower) alkyl;  
 (2,2-dimethoxymethylmorpholino) (lower) alkyl;  
 (2,3-dimethoxymethylmorpholino) (lower) alkyl;  
 (2,6-dimethoxymethylmorpholino) (lower) alkyl;  
 (2-methoxymethylmorpholino) (lower) alkenyl;  
 (3,3-dimethylmorpholino) (lower) alkynyl;  
 (2-methoxymethylmorpholino) (lower) alkynyl;  
 (2-methoxymethyl-5-methylmorpholino) (lower) alkynyl;  
 quinoly(lower) alkyl;  
 [1H-pyrrolo[3,2-b]pyridinyl] (lower) alkyl;  
 [4,5,6,7-tetrahydrothieno[3,2-c]pyridinyl] (lower) -  
 alkyl;  
 [3,4-dihydro-2H-pyrido[3,2-b]-1,4-oxazinyl] (lower) -  
 alkyl;  
 (5,6,7,8-tetrahydro-1,6-naphthyridin-6-yl) (lower) -  
 alkyl; or  
 lower alkyl which is substituted with a saturated  
 heterocyclic group of the formula :



(wherein  
 r, s and t are each integer  
 of 1 to 2, and  
 q is integer of 0 to 2)

which may be substituted with one or two lower  
 alkyl,

00957850-051204

provided that when

R<sup>4</sup> is 3-(3-pyridyl)propyl;

3-(3-pyridyl)propenyl;

pyrazolylmethyl which may be substituted with

hydroxy(lower)alkyl;

(2-methoxymethylmorpholino)(lower)alkyl;

(3-methoxymethylmorpholino)(lower)alkyl; or

(2-methoxymethylmorpholino)(lower)alkynyl, then

R<sup>2</sup> is not di(lower)alkylphenyl,

and a salt thereof.

2. The compound of claim 1, in which

Y is lower alkylene;

R<sup>1</sup> is phenyl which is substituted with 1 or 2 same

or different substituent(s) selected from the group

consisting of halogen, lower alkyl, lower alkoxy,

mono(or di or tri)halo(lower)alkyl, nitro, amino,

lower alkylamino, di(lower)alkylamino, lower

alkylthio, lower alkylsulfonyl,

cyclo(lower)alkylsulfonyl, aminosulfonyl, lower

alkylaminosulfonyl, di(lower)alkylaminosulfonyl,

pyrrolidinylsulfonyl, morpholinylsulfonyl,

pyrrolylsulfonyl, pyridylsulfonyl, pyrrolyl and  
pyridyl;

R<sup>2</sup> is phenyl which is substituted with 1 or 2 same

or different substituent(s) selected from the group

consisting of lower alkyl, mono(or di or

tri)halo(lower)alkyl, mono(or di or

tri)halo(lower)alkylsulfonyloxy, halogen, lower

alkylenedioxy, lower alkoxy, lower alkoxycarbonyl,

lower alkoxy(lower)alkoxy(lower)alkoxy, hydroxy,

diphenyl(lower)alkylsilyloxy,

tri(lower)alkylsilyloxy, hydroxy(lower)alkyl,

cyano, amino, [mono(or di or

tri)halo(lower)alkylcarbonyl]amino, lower

alkylamino, N-(lower alkyl)-[mono(or di or tri)halo(lower)alkylcarbonyl]amino, pyrrolidinyl and morpholinyl which may be substituted with lower alkoxy(lower)alkyl or lower alkyl;

5 R<sup>3</sup> is hydrogen; and

R<sup>4</sup> is 3-(3-pyridyl)propyl;

3-(3-pyridyl)propynyl;

(2,6-dimethylmorpholino)(lower)alkyl;

(3,3-dimethylmorpholino)(lower)alkyl;

10 (cis-3,5-dimethylmorpholino)(lower)alkyl;

((3S,5S)-3,5-dimethylmorpholino)(lower)alkyl;

((3S,5R)-3,5-dimethylmorpholino)(lower)alkyl;

(2-methoxymethylmorpholino)(lower)alkyl;

(3-methoxymethylmorpholino)(lower)alkyl;

15 (2-methoxymethyl-5-methylmorpholino)(lower)alkyl;

(2-methoxymethyl-5,5-dimethylmorpholino)(lower)-  
alkyl;

(3,5-dimethoxymethylmorpholino)(lower)alkyl;

(2,3-dimethoxymethylmorpholino)(lower)alkyl; or

20 (2-methoxymethylmorpholino)(lower)alkenyl,

provided that when

R<sup>4</sup> is 3-(3-pyridyl)propyl;

(2-methoxymethylmorpholino)(lower)alkyl; or

(3-methoxymethylmorpholino)(lower)alkyl, then

25 R<sup>2</sup> is not di(lower)alkylphenyl.

3. The compound of claim 2, in which

Y is C<sub>1</sub>-C<sub>4</sub> alkylene;

R<sup>1</sup> is bis[mono(or di or tri)halo(C<sub>1</sub>-C<sub>4</sub>)alkyl]phenyl;

30 R<sup>2</sup> is phenyl which is substituted with 1 or 2 same  
or different substituent(s) selected from the group  
consisting of C<sub>1</sub>-C<sub>4</sub> alkyl, mono(or di or  
tri)halo(C<sub>1</sub>-C<sub>4</sub>)alkyl, halogen, C<sub>1</sub>-C<sub>4</sub> alkoxy and  
hydroxy;

35 R<sup>3</sup> is hydrogen; and

R<sup>4</sup> is 3-(3-pyridyl)propyl;  
3-(3-pyridyl)propynyl;  
(2,6-dimethylmorpholino) (C<sub>1</sub>-C<sub>4</sub>) alkyl;  
(2-methoxymethylmorpholino) (C<sub>1</sub>-C<sub>4</sub>) alkyl;  
5 (3-methoxymethylmorpholino) (C<sub>1</sub>-C<sub>4</sub>) alkyl; or  
(2-methoxymethyl-5-methylmorpholino) (C<sub>1</sub>-C<sub>4</sub>) alkyl,

provided that when

R<sup>4</sup> is 3-(3-pyridyl)propyl;  
(2-methoxymethylmorpholino) (C<sub>1</sub>-C<sub>4</sub>) alkyl; or  
10 (3-methoxymethylmorpholino) (C<sub>1</sub>-C<sub>4</sub>) alkyl, then  
R<sup>2</sup> is not di(C<sub>1</sub>-C<sub>4</sub>) alkylphenyl.

4. A compound of claim 3, which is selected from the group consisting of

- 15 (1) 1-[3,5-Bis(trifluoromethyl)benzoyl]-2-(3-hydroxy-4-methylbenzyl)-4-[2-[(3R)-3-(methoxymethyl)morpholino]-ethyl]piperazine,
- (2) 1-[3,5-Bis(trifluoromethyl)benzoyl]-4-[2-(cis-2,6-dimethylmorpholino)ethyl]-2-(3-hydroxy-4-methylbenzyl)piperazine,
- 20 (3) 1-[3,5-Bis(trifluoromethyl)benzoyl]-2-(3-hydroxy-4-methylbenzyl)-4-[2-[(2S,5S)-2-methoxymethyl-5-methylmorpholino]ethyl]piperazine,
- (4) 1-[3,5-Bis(trifluoromethyl)benzoyl]-2-(3-hydroxy-4-methylbenzyl)-4-[3-(3-pyridyl)-2-propynyl]piperazine,
- 25 (5) 1-[3,5-Bis(trifluoromethyl)benzoyl]-4-[2-[(2S)-2-(methoxymethyl)morpholino]ethyl]-2-(3-hydroxy-4-methylbenzyl)piperazine,
- (6) (2R)-1-[3,5-Bis(trifluoromethyl)benzoyl]-4-[2-[(2S)-2-(methoxymethyl)morpholino]ethyl]-2-(3-hydroxy-4-methylbenzyl)piperazine,
- 30 (7) 1-[3,5-Bis(trifluoromethyl)benzoyl]-2-(3-hydroxy-4-methylbenzyl)-4-[3-(3-pyridyl)propyl]piperazine,
- (8) (2R)-1-[3,5-Bis(trifluoromethyl)benzoyl]-2-(4-chloro-3-hydroxybenzyl)-4-[2-[(2S)-2-(methoxymethyl)morpholino]-
- 35

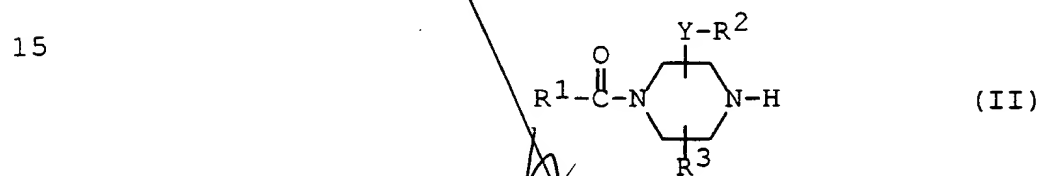
ethyl]piperazine,

(9) (2R)-1-[3,5-Bis(trifluoromethyl)benzoyl]-2-(4-fluoro-3-methoxybenzyl)-4-[2-[(2S)-2-(methoxymethyl)morpholino]-ethyl]piperazine, and

5 (10) (2R)-1-[3,5-Bis(trifluoromethyl)benzoyl]-2-[4-(trifluoromethyl)benzyl]-4-[2-[(2S)-2-(methoxymethyl)-morpholino]ethyl]piperazine,  
or a pharmaceutically acceptable salt thereof.

10 5. A process for the preparation of the compound of claim 1 or a salt thereof, which comprises,

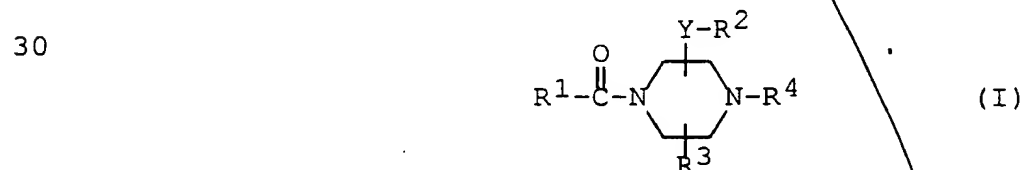
(1) reacting a compound of the formula (II) :



20 wherein  $R^1$ ,  $R^2$ ,  $R^3$  and Y are each as defined in claim 1, or a salt thereof, with a compound of the formula (III) :



25 wherein  $R^4$  is as defined in claim 1 and  $W_1$  is a leaving group,  
or a salt thereof to give a compound of the formula (I) :

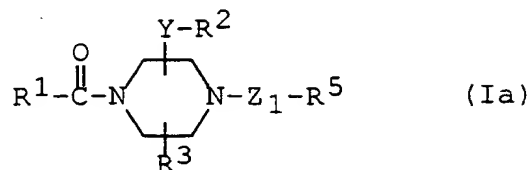


35 wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$  and Y are each as defined in

claim 1,

or a salt thereof, or

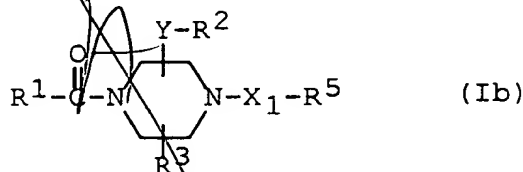
(2) subjecting a compound of the formula (Ia) :



wherein  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$  and Y are each as defined above,  
 $\text{R}^5$  is 3-pyridyl, and

$\text{Z}_1$  is lower alkynylene,

or a salt thereof to a reduction reaction to give a  
 compound of the formula (Ib) :



wherein  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ , Y and  $\text{R}^5$  are each as defined above,  
 and

$\text{X}_1$  is lower alkylene,

or a salt thereof.

6. A pharmaceutical composition which comprises, as an  
 active ingredient, a compound of claim 1 or a  
 pharmaceutically acceptable salt thereof in admixture  
 with pharmaceutically acceptable carriers.

7. A compound of claim 1 for use as a medicament.

8. A method for treating or preventing Tachykinin-mediated  
 diseases which comprises administering an effective

amount of a compound of claim 1 or a pharmaceutically acceptable salt thereof to human being or animals.

9. A compound of claim 1 for use as Tachykinin antagonist.
10. Use of a compound of claim 1 for manufacture of a medicament for treating or preventing Tachykinin-mediated diseases.

5

[illegible]

add  
A1